

## REMARKS

Claims 11, 13, 31, 32, 34, 35, and 38 are as previously presented, and claims 33 and 36 are as originally filed. Claims 7, 12, and 15-30 were previously canceled. Claims 1-6, 7-10, 14, 37, and 39 were amended; however, no new matter has been introduced.

New claim 40 is added; however, no new matter is introduced. Support for claim 40 can be found in claim 1 as previously presented.

With these amendments, claims 1-6, 8-11, 13, 14, and 31-40 are pending.

### **Rejections under 35 U.S.C. § 112, first paragraph**

Claims 1-6, 8-11, 13, 14, and 31-39 stand rejected under 35 U.S.C. § 112, first paragraph, for reciting “cyanato, thiocyanato, selenocyanato, trifluoromethoxy, and azido”. The Office alleges that these terms are new matter and not supported by the application as filed. Applicants respectfully disagree.

The Office rejected the term “pseudohalo” in the Office action mailed March 5, 2009. In response to this rejection, Applicants replaced the term “pseudohalo” with the terms “cyanato, thiocyanato, selenocyanato, trifluoromethoxy, and azido”. This amendment was fully supported by the specification as filed and did not constitute new matter. The non-valent counterpart to pseudohalo is pseudohalide. Pseudohalide is defined at page 18, line 8 of the specification:

“As used herein, pseudohalides or pseudohalo groups are groups that behave substantially similar to halides. Such compounds can be used in the same manner and treated in the same manner as halides. Pseudohalides include, but are not limited to, cyanide, cyanate, thiocyanate, selenocyanate, trifluoromethoxy, and azide.”

(Emphasis added). Hence, the term “pseudohalo” includes “cyanato, thiocyanato, selenocyanato, trifluoromethoxy, and azido” groups. Amending “pseudohalo” to recite these groups is clear to a person of skill in the art, fully supported by the specification and does not constitute new matter.

Applicants respectfully request reconsideration and withdrawal of 35 U.S.C. § 112, first paragraph rejections.

### **Rejections under 35 U.S.C. § 112, second paragraph**

A. Claims 1-6, 8-11, 13, 14, and 31-39 stand rejected under 35 U.S.C. § 112, second paragraph, for omitting the definition of R<sup>7</sup>. In response, Applicants amended the claims to insert

the definition of R<sup>7</sup>, which was inadvertently deleted in the amendment submitted on August 5, 2009. Support for defining R<sup>7</sup> is found in originally filed claims, and throughout the specification (e.g., page 7, line 19).

B. Claims 1-6, 8-11, 13, 14, and 31-39 stand rejected under 35 U.S.C. § 112, second paragraph, for reciting mono-valent moieties in the definition of R<sup>12</sup> and reciting C<sub>1</sub> alkenyl and alkynyl. Applicants respectfully disagree and note that a person of skill in the art would understand that R<sup>12</sup> is a divalent moiety and that the recited alkyl, alkenyl, etc. would satisfy the two-bond requirement (e.g., alkylene is a subset of alkyl). Nevertheless, Applicants clarified the definition of R<sup>12</sup>, which now recites “C<sub>1</sub>-C<sub>6</sub> alkylene, C<sub>2</sub>-C<sub>6</sub> alkenylene, C<sub>2</sub>-C<sub>6</sub> alkynylene or C<sub>1</sub>-C<sub>6</sub> alkylenoxy”. This amendment is fully supported by the specification as filed; in particular, pages 18 and 19.

Applicants respectfully request reconsideration and withdrawal of 35 U.S.C. § 112, second paragraph rejections.

#### **Rejections under 35 U.S.C. § 102**

Claims 1-6, 8-11, 13, 14, and 31-39 stand rejected under 35 U.S.C. § 102(a), (b), and (e) as being unpatentable over numerous references and myriad compounds. As explained below, the cited art does not anticipate the claims presented herein.

The Office argues that Ahmad (US 6887870) recites a composition of compounds where one of R<sup>2</sup> and R<sup>4</sup> is halogen and the other is heterocycle and that the 4- and 6- positions on the pyrimidine ring are equivalent. But in the present claims R<sup>2</sup> cannot be heterocycle or halogen. Therefore, the claims are not anticipated by Ahmad.

The Office again argues that Chu-Moyer (US 6414149) reads on the claims because Chu-Moyer recites a composition comprising a compound where one of R<sup>2</sup> and R<sup>4</sup> is hydrogen and the other is heterocycle and the positions corresponding to R<sup>2</sup> and R<sup>4</sup> are equivalent. But R<sup>2</sup> cannot be heterocycle or hydrogen in the present claims. Therefore, the claims are not anticipated by Chu-Moyer.

Kinoshita (WO 2000/041999) recites an insecticide and not a pharmaceutical composition. Thus, Kinoshita does not anticipate the claims. Even though the Office argues that one of the substituents corresponding to R<sup>2</sup> and R<sup>4</sup> is hydrogen and that these positions are interchangeable, the present claims recite compounds where neither R<sup>2</sup> nor R<sup>4</sup> can be hydrogen.

The Office again argues that a composition of Murata (JP 2001/139560) reads on the claims because Murata recites a composition of compounds where one of R<sup>2</sup> and R<sup>4</sup> is halogen and the other is aryl and the positions corresponding to R<sup>2</sup> and R<sup>4</sup> are equivalent. But R<sup>2</sup> cannot be aryl or halogen in the present claims. Therefore, the claims are not anticipated by Murata.

Nunes (WO 2005/009443) recites a composition of compounds where one of R<sup>2</sup> and R<sup>4</sup> is hydrogen and the other is aryl. Even though the Office argues that the substituents R<sup>2</sup> and R<sup>4</sup> of Kinoshita are interchangeable, the present claims recite compositions of compounds where R<sup>2</sup> cannot be aryl or hydrogen. Therefore, the claims are not anticipated by Nunes.

Gutheil (US 2002/0004600) teaches a process for preparation of compounds. There is no disclosure of a pharmaceutically acceptable composition or a preparation in a pharmaceutically acceptable vehicle. In addition, the compounds disclosed in Gutheil require one of the substituents corresponding to R<sup>2</sup> and R<sup>4</sup> to be hydrogen and that these positions are interchangeable. But, the present claims recite compounds where neither R<sup>2</sup> nor R<sup>4</sup> can be hydrogen. Thus, Gutheil does not anticipate the claims.

Bebbington (WO 2002/022606) and Bebbington (WO 2002/022608) disclose compound RN 404827-83-4, in which the one of the moieties corresponding to R<sup>2</sup> and R<sup>4</sup> is halogen and the other cycloalkyl. The presently amended claims recite compositions where neither R<sup>2</sup> nor R<sup>4</sup> can be halogen. The remaining compounds of Bebbington do not fall with the present claims because neither R<sup>2</sup> nor R<sup>4</sup> can be halogen, alkyl, or a substituted amino group (e.g., pyrazolyl-NH-). Therefore, the claims are not anticipated by either Bebbington reference.

Davey (US 6127376) recites compositions of compounds that require both R<sup>2</sup> and R<sup>4</sup> to be phenoxy; but in the present claims only the definition of R<sup>2</sup> includes an -OR<sup>6</sup> moiety. Therefore most of compositions of Davey do not fall within the scope of the claims. One composition comprises compound RN 274673-44-8, where one of the substituents corresponding to R<sup>2</sup> and R<sup>4</sup> is halogen and the other is phenoxy. R<sup>2</sup> or R<sup>4</sup> cannot be halogen in the presently amended claims, so Davey cannot anticipate.

Sugiura (JP 11158073) recites compositions of compounds where at least one of R<sup>2</sup> and R<sup>4</sup> is substituted amino (e.g., cyclohexylamino). Neither R<sup>2</sup> nor R<sup>4</sup> allow for amino substitution of the pyrimidine ring. Therefore, the claims are not anticipated by Sugiura.

Brown (WO 1998/23155) discloses agriculturally suitable fungicides. There is no disclosure of a pharmaceutically acceptable composition or a formulation in a pharmaceutically

acceptable vehicle. In addition, Brown recites a compound where one of  $R^2$  and  $R^4$  is hydrogen and the other is aryloxy and the positions corresponding to  $R^2$  and  $R^4$  are equivalent. But  $R^4$  cannot be hydrogen or aryloxy in the present claims. Thus, Brown does not anticipate the claims.

Like Brown above, Walker (WO 1998/20003) disclose agriculturally suitable fungicides. There is no disclosure of a pharmaceutically acceptable composition or a formulation in a pharmaceutically acceptable vehicle. In addition, Walker recites a compound where one of  $R^2$  and  $R^4$  is hydrogen and the other is aryloxy and the positions corresponding to  $R^2$  and  $R^4$  are equivalent. But  $R^4$  cannot be hydrogen or aryloxy in the present claims. Thus, Walker does not anticipate the claims.

Kleemann (US 5849758) and Kleemann (US 5824624) disclose herbicides. There is no disclosure of a pharmaceutically acceptable composition or a formulation in a pharmaceutically acceptable vehicle in either reference. In addition, these references recite compounds that require  $R^4$  to be methoxymethyl; but in the present claims the definition of  $R^4$  can not be an  $-R^{12}-OR^{13}$  moiety. The remaining compounds of Kleemann do not fall with the present claims because neither  $R^2$  nor  $R^4$  can be halogen, alkyl, alkenyl, alkynyl, alkylthio, or a substituted amino group (e.g., Me-NH-). Thus, Kleemann references do not anticipate the claims.

Munro (US 5707995) discloses a pesticide. There is no disclosure of a pharmaceutically acceptable composition or a formulation in a pharmaceutically acceptable vehicle. In addition, Munro recites compounds that require both  $R^2$  and  $R^4$  to be phenoxy; but in the present claims only the definition of  $R^2$  includes an  $-OR^6$  moiety. Thus, Munro does not anticipate the claims.

Ohkubo (Chem. Pharm. Bull. (1994) 42(6), 1279-1285) discloses compositions of compounds wherein  $R^3$  is 4-methylpiperazin-1-ylcarbonyl, hydroxycarbonyl, or ethoxycarbonyl. None of these groups fall within the scope of the definition of  $R^3$  in the present claims. In addition, in the compounds in the compositions of Ohkubo either  $R^2$  or  $R^4$  is hydrogen or alkyl, neither which is allowed by the present claims. Thus, the claims are not anticipated by Ohkubo.

Clough (EP 468695) discloses agriculturally suitable fungicides. There is no disclosure of a pharmaceutically acceptable composition or a formulation in a pharmaceutically acceptable vehicle in Clough. In addition, Clough discloses a compound where one of  $R^2$  and  $R^4$  is hydrogen and the other is aryloxy and the positions corresponding to  $R^2$  and  $R^4$  are equivalent. But  $R^4$  cannot be hydrogen or aryloxy in the present claims. Therefore, the claims are novel with respect to Clough.

El-Bahaie (Pharmazie (1991) 46(1), 26-28) discloses a few compositions of compounds where  $R^3$  is acetate, which is not allowed by the presently claimed definition of  $R^3$ . In addition, all compositions recite compounds in which  $R^4$  is alkyl, and the present claims recite compositions of compounds where  $R^4$  cannot be alkyl. Thus, the claims are not anticipated by El-Bahaie.

El-Kerdawy (Archives of Pharmaceutical Research (1990) 13(2), 142-146) discloses compositions of compounds wherein  $R^3$  is hydroxycarbonyl or ethoxycarbonyl. Neither one of these two groups are allowed by the definition of  $R^3$  of the present claims. In addition, the compositions of El-Kerdawy comprise compounds in which  $R^4$  is hydrogen, which is not allowed by the claims.

Kampe (US 4859670) discloses compositions of compounds where one of  $R^2$ ,  $R^3$ , and  $R^4$  is phenol-substituted piperazinylmethyl. A phenol substituent on a piperazinylmethyl group is not allowed by the definition of  $Q^1$  in the present claims. Thus, the majority of compositions of Kampe do not fall within the scope of the claims. One composition of Kampe comprises compound RN 111921-72-3, which recites that one of substituents  $R^2$  and  $R^4$  is methoxy and the other is alkyl. The present claims recite compositions comprising compounds in which neither  $R^2$  or  $R^4$  is alkyl.

Burdeska (US 4493726) discloses agriculturally suitable herbicides, and Seiler (EP 0136976) discloses compounds for regulating plant growth. There is no disclosure of a pharmaceutically acceptable composition or a formulation in a pharmaceutically acceptable vehicle in Burdeska or in Seiler. In addition, none of the compounds cited in either reference fall within the scope of the claims because neither  $R^2$  nor  $R^4$  can be halogen, alkyl, or a substituted amino group; nor can both  $R^2$  and  $R^4$  be  $-OR^6$ . Thus, the claims are not anticipated by Burdeska and in Seiler.

Cirillo (WO 2002/092576) recite compositions of compounds where one of the moieties corresponding to  $R^2$  and  $R^4$  is hydrogen and the other is aryloxy. But  $R^4$  cannot be hydrogen in the present claims. In addition, the aryloxy group in the definition of  $Q^1$  in the present claims cannot be substituted.

For all of the above reasons, Applicants submit that the claims are not anticipated by the cited references. Reconsideration and withdrawal of rejections under 35 U.S.C. § 102(a), (b), and (c) is respectfully requested.

**Rejections under 35 U.S.C. § 103(a)**

Claims 1-6, 8-11, 13, 14, and 31-39 stand rejected under 35 U.S.C. § 103(a) as being obvious over several references. Applicants respectfully disagree for the following reasons:

The Office cited Gutheil (US 2002/0004600) and asserted that the “claimed compounds are alkyl homologs and/or position isomers of the Gutheil compounds and obvious to the skilled chemist for the same utility.” (Office Action p. 12, l. 15-16). In the discussion of prior art, Gutheil broadly states that the certain pyrimidines are of great interest (see paragraph [0002]). However, Gutheil does not teach or suggest that the compounds prepared according to the disclosed methods are pharmaceutically useful. There is no suggestion that the compounds of Gutheil are formulated for pharmaceutical use or that they might have activity in the Gal4-chimera-reporter gene assay like the composition of compounds recited in the present claims. Thus, one of skill in the art would not conclude that the compositions recited in the claims would be obvious based on the compounds prepared by the methods of Gutheil.

The Office asserts that the compounds of Bebington (WO 2002/022606), Bebington (WO 2002/022608), Davey (US 6127376), Sugiura (JP 11158073), Ohkubo (Chem. Pharm. Bull (1994) 42(6), 1279-1285), El-Bahaie (Pharmazie (1991) 46(1), 26-28), El-Kerdawy (Archives of Pharmaceutical Research (1990) 13(2), 142-146), Kampe (US 4859670), and Cirillo (WO 2002/092576) are alkyl homologs and/or position isomers of the claimed compounds, and thus obvious to the skilled chemist for the same utility. The compounds of prior art are not alkyl homologs and/or positional isomers of the claimed compounds. Thus, the compounds of the prior art are not similar structures and not expected to have similar properties to those claimed. A person of skill in the art would not be motivated to modify the prior art compounds to arrive to the presently claimed matter based on the teaching of the above-listed references.

In addition, the present application includes biological activity data of the claimed compositions in Figures 1A-1O that demonstrate the activity in Gal4-chimera-reporter gene assay. These results indicate that the claimed compositions show significant activity in this assay. Figures 2, 3, 4A and 4B disclose additional biological activity. For example, Figures 4A and 4B show that the claimed compositions are able to selectively activate Nurrl/RXR heterodimers but have minimal ability to directly activate RXR. The prior art does not teach that the compounds disclosed therein have activity in Gal4-chimera-reporter gene assay or that they are able to selectively activate Nurrl/RXR heterodimers. There is nothing in the prior art that

would make obvious to one of skill in the art that the compounds of the prior art could or should be modified in a manner that results in the compounds recited in the present claims or that such compounds would have activity in the Gal4-chimera-reporter gene assay.

Brown (WO 1998/23155), Walker (WO 1998/20003), Kleemann (US 5849758), Kleemann (US 5824624), Clough (EP 468695), Burdeska (US 4493726), Munro (US 5707995), and Seiler (EP 0136976) disclose compounds which are fungicides, herbicides, pesticides, or regulators of plant growth. None of these references disclose or suggest pharmaceutically acceptable compositions or formulations in a pharmaceutically acceptable vehicle. The teachings of these references are insufficient to make the presently claimed pharmaceutical composition obvious because there is no suggestion that the fungicidal/herbicidal/pesticide composition could or should be modified in a manner to give a pharmaceutical composition. Nor is there anything in the art to suggest that the fungicidal/herbicidal/pesticide composition would have pharmaceutical utility.

Therefore, one of skill in the art, having either one of these references at hand, would not arrive at the claimed compositions. As a result, reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. 103(a) is respectfully requested.

### **Objectionable Claims**

Claims 1-11, 13, 14, and 31-36 were objected to as directed to both elected and non-elected subject matter. Applicants amended the claims in the Response submitted on August 5, 2009 to remove the non-elected matter. The current claims recite only elected subject matter; claim 7 is not pending. Applicants respectfully request withdrawal of the claim objections.

In light of the all above arguments, the Applicant respectfully requests reconsideration and withdrawal of the rejections of the pending claims. If the Examiner believes it to be helpful, the Examiner is invited to contact the undersigned representative by telephone at (312) 913-0001.

Respectfully submitted,

Date: July 27, 2010

/Jelena Janjic Libby/  
Jelena Janjic Libby  
Registration No. 64,347

Telephone: 312-913-0001  
Facsimile: 312-913-0002

**McDonnell Boehnen Hulbert & Berghoff LLP**  
300 South Wacker Drive  
Chicago, IL 60606